UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/451,527 | 12/01/99 | SIM G | IM-2-C2 |

026949
HESKA CORPORATION
INTELLECTUAL PROPERTY DEPT.
1613 PROSPECT PARKWAY
FORT COLLINS CO 80525

HM12/0706

| EXAMINER | |
|---|---|
| KAUSHAL, S | |
| **ART UNIT** | **PAPER NUMBER** |
| 1633 | 8 |

**DATE MAILED:** 07/06/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/451,527 | Applicant(s) SIM ET AL. | |
|---|---|---|---|
| | Examiner Sumesh Kaushal | Art Unit 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-17,20,22,25 and 29-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,19,21,23,24 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election without traverse of Group-20, claims 18-19, 21, 23-24 and 26-28 in Paper No. 7 is acknowledged. Claim 21 drawn to an isolated Canine IL-13 protein and therefore is included in Group-20.

Claims 1-17, 20, 22, 25 and 29-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

### *Claim Objections*

Claims 18-19, 21, 23-24 and 26-28 are objected to because of the following informalities: The instant claims contain non-elected subject matter. The instant claims are examined only to the extent that it encompasses the elected subject matter (Canine IL-13 protein). Appropriate correction is required.

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 18-19, 21, 23-24 and 26-28 are rejected under 35 U.S.C. 101 because the claimed **invention lacks patentable utility**.

The instant claims are drawn to an isolated protein consisting of at least 15 amino acids in length encoded by at least 45 contiguous nculeotide region identical in sequence to a 60 contiguous neucleotide region selected from SEQ ID NO: 88, 89, 90, 91, 94, 96, 99, 102 and 104. The claims are drawn to an isolated protein of 15 amino acids wherein the protein has an at least 15 contiguous amino acid region identical to SEQ ID NO: 92, 97, 100 and 105. The claims are drawn to the isolated protein, which elicits an immune response against Canine IL-13 protein or has IL-13 activity. The claims are drawn to allelic variant of a nucleic acid molecule encoding a protein selected from SEQ ID NO: SEQ ID NO: 92, 97, 100 and 105. The claims are drawn to an isolated protein having 70% identity to amino acid sequences of SEQ ID NO: SEQ ID NO: 92, 97, 100 and 105. In addition, the claims are drawn to a therapeutic composition and a method to regulate an immune response in an animal by administering an isolated protein consisting of at least 15 amino acids in length encoded by at least 45 contiguous nculeotide region identical in sequence to a 45 contiguous neucleotide region selected from SEQ ID NO: : 88, 89, 90, 91, 94, 96, 99, 102 and 104 and isolated protein of 15 amino acids wherein the protein has an at least 15 contiguous amino acid region identical to SEQ ID NO: 92, 97, 100 and 105, wherein the protein elicits an immune response against Canine IL-13 protein or has IL-13 activity

The instant invention is not considered to have a specific and/or substantial utility because the specification fails to establish that the disclosed polynucleotide sequences encodes an amino acid, which is an IL-13 like protein as shown by structural and functional properties. The recited SEQ ID NO(s) are simply computer-generated hypotheses, wherein no biological function has been established. It is known in the art that IL-13 have very divergent functions. For example, IL-13 is pleiotropic cytokine, which promotes growth and differentiation of B cells, up regulation of MHC class II and CD23 expression on monocytes/macrophages and B cells, and inhibit the production of inflamatory cytokines such as IL1a, IL-1b, IL-6, IL-8, IL-10 and IL-12 (Minty et al, Nature 362:248-250, 1993; specification, page 2 line 17-20). The specification fails to show a single working example that establishes that the instant polynucleotide encodes an amino acid sequence having IL-13 like activity, such as by substantial sequence homology and/or functional assay of the protein. The specification alleges that the instant nucleic acid encodes for a Canine IL-13 like protein. However, no sequence comparisons are taught by

specification as filed, nor are any specific similarities to other members of IL-13 proteins are disclosed, such as common areas of conservation. The specification fails to teach that polypeptide encoded by claimed SEQ ID NO: 88, 89, 90, 91, 94, 96, 99, 102 and 104 have the biological activity of IL-13 explicitly or implicitly as putatively considered by the specification. The only immediate apparent utility for the instant invention would be its further scientific characterization as a putative IL-13 like protein isolated form a canine. In view of the foregoing, one skilled in the art would not readily attribute IL-13-like activity encoded by the instant nucleic acid in view of the low sequence similarity and the lack of sequence conservation therein. In view of such and the fact that IL-13 differ substantially in activity, it is unclear that IL-13 like activity could be attributed to the deduced amino acid sequence of the claimed nucleic acid. The office sequence search using the disclosed amino acid sequences provided only one match with the human IL-13 (AN:A47481), but with only with 68-69% amino acid sequence similarity. Further inspection of the comparison shows limited if any areas of conservation between the two sequences.

It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The recited SEQ ID NO(s) are simply computer generated hypothesis because no biological functions has been established. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. Therefore, the asserted use for the claimed nucleic acid is not considered to support by either a specific and/or substantial utility, since no function can be ascribed to the gene.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-19, 21, 23 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession of the claimed invention**.

The instant claims are drawn to an isolated protein consisting of at least 15 amino acids in length encoded by at least 45 contiguous nculeotide region identical in sequence to a 60 contiguous neucleotide region selected from SEQ ID NO: 88, 89, 90, 91, 94, 96, 99, 102 and 104. The claims are drawn to an isolated protein of 15 amino acids wherein the protein has an at least 15 contiguous amino acid region identical to SEQ ID NO: 92, 97, 100 and 105. The claims are drawn to the isolated protein, which elicits an immune response against Canine IL-13 protein or has IL-13 activity. The claims are drawn to allelic variant of a nucleic acid molecule encoding a protein selected from SEQ ID NO: SEQ ID NO: 92, 97, 100 and 105. The claims are drawn to an isolated protein having 70% identity to amino acid sequences of SEQ ID NO: 92, 97, 100 and 105. In addition, the claims are drawn to a therapeutic composition and a method to regulate an immune response in an animal by administering an isolated protein consisting of at least 15 amino acids in length encoded by at least 45 contiguous nculeotide region identical in sequence to a 45 contiguous neucleotide region selected from SEQ ID NO: : 88, 89, 90, 91, 94, 96, 99, 102 and 104 and isolated protein of 15 amino acids wherein the protein has an at least 15 contiguous amino acid region identical to SEQ ID NO: 92, 97, 100 and 105, wherein the protein elicits an immune response against Canine IL-13 protein or has IL-13 activity

The invention as claimed encompasses any and all variants of IL-13 protein. At best the specification only discloses amino acid sequences of SEQ ID NO: 92, 97, 100 and 105, which elicits TF-1 proliferation activity (spec. page 154, table-6). The specification proposes to

discover other members of the genus using hybridization procedure or sequence similarity. However, there is no description of mutational sites that exist in nature, and there is no description how the structure of identified nucleic acid sequences relates to the structure of any strictly neutral alleles. In addition, the IL-13-like polypeptide includes members that would expect to have widely divergent functional properties. The general knowledge in the art concerning IL-13-like protein does not provide any indication as how the structure of one allele is representative of other unknown amino acid sequences having concordant or discordant functions. The commons attributes of the IL-13 protein are not described, and identifying attributes of individual IL-13-like protein other than SEQ ID NO(s) as claimed are not described. The nature of IL-4-like protein is that they are variant structures and functions of others. The specification only disclosed nucleic and amino acid sequences encoding Canine IL-3 polypeptide. The specification fails to describe any and all nucleic and amino acid sequences encoding IL-13-like protein obtained from any other animal. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claims 18-19, 21, 23-24 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, **to make and/or use the invention**.

The claimed invention is described above in written description rejection. The invention as claimed encompasses any and all variants of IL-13 protein isolated from any and all animals. At best the specification discloses that E. coli produced Canine-pCaIL1-3 recombinant protein stimulate the proliferation of TF-1 cells (page 154, table-6). The specification teaches that putative IL-4 (pg 125, table-3), IL-5(pg 148, table-5) also promotes the proliferation of TF-1 cells. The art at the time of filing teaches that TF-1 cell line is know to proliferate to a wide variety of cytokines (McKenzie et al, PNAS, 90:3735-3739, 1993). Therefore it is unclear whether the isolated proteins as claimed have any IL-13 specific activity. Similarly, it is unclear

whether the polypeptide encoded by any and all variants of claimed SEQ ID NO(s) have the biological activity of IL-13 explicitly or implicitly as putatively considered by the specification

The invention as claimed encompass a protein of at least 15 amino acid in length identical to the amino acid sequences of SEQ ID NO: 92, 97, 100 and 105 and a protein encoded by at least 45 nucleotides identical to SEQ ID NO: 88, 89, 90, 91, 94, 96, 99, 102 and 104, wherein the protein elicits an immune response against Canine IL-13 protein or has IL-13 activity. In addition, the invention as claimed encompass 30% amino acid sequence variation over the entire length of SEQ ID NO: 92, 97, 100 and 105 (claim 21). The variation also encompasses the conserved motifs that are germane to the IL-13 specific biological activity. It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The recited SEQ ID NO(s) are simply computer-generated hypothesis because no biological function has been established. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. Therefore, Applicant has not presented enablement commensurate in scope with the claims.

Furthermore, it is unclear how one skill in the art would use any and all variants (as claimed) to regulate an immune response in an animal which is specific to Canine IL-13 protein or IL-13 activity. The art the time of filing teaches that Inteleukin-13 is involved in the regulation of Th2 immune response. IL-13 and IL-4 act in combination to ensure the rapid onset of Th2 like response. In addition, regulation and effects of Th2 response is complex which involves molecular and cellular interactions. Th2 cytokine response (IL-4, IL-5, IL-9 and IL-13) is involved in immune rejections of parasite helminth infections, allergies and asthema. Th2 can mediate protective immunity to worm infection but inappropriate inflammatory response leads allergic challenge (McKenzie, Pharma. Ther. 88:143-151, 2000). Considering the specific role of the IL-13 interaction in Th2 response, it is unclear how one skill in the art would use the

claimed SEQ ID NO(s) or its variants without further undue experimentation. Therefore, further characterization of any and all putative variants of IL-4 is germane to exercise the invention as claimed.

Thus, in view of lack of specific guidance in the specification, the skilled artesian at the time of filing would be unable to use the claimed invention, without an excessive and undue amount of experimentation. The quantity of experimentation required would include making and functional characterization of any and all variants as IL-13-like protein from any and all animals that elicits an immune response against IL-13 protein or has IL-13 activity.

***Conclusion***

No claims are allowed.

Claims 18-19, 21, 23-24 and 26-28 are free of prior art. The prior art of record does not teach or suggest an isolated Canine IL-13 comprising the nucleic acid sequence of SEQ ID NO: 88, 89, 90, 91, 94, 96, 99, 102 and 104 which encodes the amino acid sequences of SEQ ID NO: 92, 97, 100 and 105.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Deborah Clark can be reached on (703) 305-4051. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Tracey Johnson, whose telephone number is (703) 308-0377. If the claims are amended canceled and/or added the applicants are required to follow Amendment Practice under 37 CFR § 1.121 *(http://www.uspto.gov)* and A CLEAN COPY OF ALL PENDING CLAIMS IS REQUESTED to facilitate further examination.

SUMESH KAUSHAL
PATENT EXAMINER